PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

To:

see form PCT/ISA/220

PCT

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

(PCT Rule 43*bis*.1)

Date of mailing
(day/month/year) see form PCT/ISA/210 (second sheet)

Applicant's or agent's file reference
see form PCT/ISA/220

FOR FURTHER ACTION
See paragraph 2 below

International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/GB2004/001383	25.03.2004	25.03.2003

International Patent Classification (IPC) or both national classification and IPC
C12N9/02

Applicant
NEUTEC PHARMA PLC

1. This opinion contains indications relating to the following items:

- ☒ Box No. I Basis of the opinion
- ☒ Box No. II Priority
- ☒ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☐ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☐ Box No. VI Certain documents cited
- ☐ Box No. VII Certain defects in the international application
- ☐ Box No. VIII Certain observations on the international application

2. **FURTHER ACTION**

If a demand for international preliminary examination is made, this opinion will usually be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA"). However, this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notifed the International Bureau under Rule 66.1*bis*(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of three months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

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WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/GB2004/001383

Box No. I Basis of the opinion

1. With regard to the **language**, this opinion has been established on the basis of the international application in the language in which it was field, unless otherwise indicated under this item.

   ☐ This opinion has been established on the basis of a translation from the original language into the following language , which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).

2. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:

   a. type of material:

   ☒ a sequence listing

   ☐ table(s) related to the sequence listing

   b. format of material:

   ☒ in written format

   ☒ in computer readable form

   c. time of filing/furnishing:

   ☒ contained in the international application as filed.

   ☒ filed together with the international application in computer readable form.

   ☐ furnished subsequently to this Authority for the purposes of search.

3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

4. Additional comments:

Box No. II Priority

1. ☒ The following document has not been furnished:

   ☒ copy of the earlier application whose priority has been claimed (Rule 43*bis*.1 and 66.7(a)).

   ☐ translation of the earlier application whose priority has been claimed (Rule 43*bis*.1 and 66.7(b)).

   Consequently it has not been possible to consider the validity of the priority claim. This opinion has nevertheless been established on the assumption that the relevant date is the claimed priority date.

2. ☐ This opinion has been established as if no priority had been claimed due to the fact that the priority claim has been found invalid (Rules 43*bis*.1 and 64.1). Thus for the purposes of this opinion, the international filing date indicated above is considered to be the relevant date.

3. Additional observations, if necessary:

Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application,

☒ claims Nos. 17, with respect to industrial applicability

because:

☐ the said international application, or the said claims Nos. relate to the following subject matter which does not require an international preliminary examination *(specify)*:

☐ the description, claims or drawings *(indicate particular elements below)* or said claims Nos. are so unclear that no meaningful opinion could be formed *(specify)*:

☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

☒ no international search report has been established for the whole application or for said claims Nos. 17

☐ the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that:

the written form	☐	has not been furnished
	☐	does not comply with the standard
the computer readable form	☐	has not been furnished
	☐	does not comply with the standard

☐ the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with the technical requirements provided for in Annex C-*bis* of the Administrative Instructions.

☒ See separate sheet for further details

Box No. V Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	1-9, 11-25
	No:	Claims	10
Inventive step (IS)	Yes:	Claims	1-9, 19
	No:	Claims	11-18, 20-25
Industrial applicability (IA)	Yes:	Claims	1-16, 18-25
	No:	Claims	

2. Citations and explanations

see separate sheet

Ad Section III: Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

Claim 17 relates to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. In this respect the following should be noted:

For the assessment of this claim on the question whether it is industrially applicable, no unified criteria exist in the PCT. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.

Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of these claims (Article 34(4)(a)(I) PCT).

Ad Section V: Reasoned statement with regard to novelty, inventive step or industrial applicability

1) The present application relates to a *Clostridium difficile* lactate dehydrogenase. The enzyme was characterised and cloned from a *C. difficile* genomic library. Antibodies reacting with the enzyme were found in the serum of patients suffering from *C. difficile* infection. Use of the enzyme as well as an antibody specifically directed to it in medical and diagnostic applications is foreseen.

2) **Novelty**

2.1) **Claim 10** which is directed to an antibody specific against a *C. difficile* lactate dehydrogenase does not meet the requirements of Art. 33(2) PCT. From the application, p. 25, lines 2-3, it can be taken that a commercially available antibody reacted with the *C. difficile* enzyme of the application. Hence the antibody as defined in **claim 10** cannot be considered novel over this commercial antibody.

2.2) Claims directed to the enzyme itself and to the nucleic acid molecule encoding the enzyme, vectors, host cells, etc. (**claims 1-9**) are considered to meet the requirements of Art. 33(2)(3) PCT as the specific enzyme was not disclosed in nor

derivable in an obvious manner from the prior art.

2.3) Novelty can also be acknowledged for the claims directed to medicaments, diagnostic methods and methods of manufacture of a medicament (**claims 11-25**).

3) Inventive step

3.1) Inventive step, however, cannot be acknowledged for **claims 11-18 and 20-25** for the following reasons:

These claims are based on the assumption that the newly discovered protein, which is recognised by antibodies present in the sera of patients suffering from *C. difficile* infection, may be involved in *C. difficile* pathogenicity. Applicants, however, provide no examples or evidence that the combination of an antibiotic and a specific lactate dehydrogenase antibody (which has not even been disclosed) shows any beneficial effects in the treatment of *C. difficile* infection as compared to traditional antibiotics.

Demonstrated function of a newly identified protein, however, is a prerequisite to the final assessment of inventive step of claims **11-17 and 20-25.**

3.2) **Claims 18, 20 and 21** do not meet the requirements of Art. 33(3) PCT for the following reasons:

Claim 18 is directed to a diagnostic method for detecting the presence in a sample of C. difficile lactate dehydrogenase using an antibody or an antibody binding fragment specific against said enzyme. As antibodies specific for the claimed enzyme are known in the art (see par. 2.1) using such antibodies in a diagnostic method is not considered to involve an inventive step.